R E M A R K S

Claims 7 and 12-17 are pending and await further action on the merits. Applicants note with appreciation that the Examiner has indicated claims 16 and 17 as being allowed.

Issues under 35 U.S.C. 103

Claims 7 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaspersen et al. (Journal of Labelled Compounds and Radiopharmaceuticals, Vol. XXVII, No.9, pages 1055-1068, 1989). Applicants respectfully traverse the rejection.

The Examiner asserts at page 3, lines 9-10 of the Office Action, that the labeled hydrate would clearly suggest the unlabeled hydrate. Applicants respectfully disagree with the Examiner's assertion.

The present inventors have for the first time found out the hydrates of an unlabeled compound. Moreover, they have for the first time found out anhydrous mirtazapine crystals having low hygroscopic properties and a high purity by drying the hydrates of an unlabeled compound, as explained at page 8, lines 12-14 of the present specification. In other words, they have for the first time found out that the hydrates are important intermediates for preparing anhydrous mirtazapine crystals.

Kaspersen et al. disclose the preparation of labeled compounds. Kaspersen et al. also disclose that:

> "[f]or metabolic studies in animal and man and for the determination of the bioavailability, the compound labeled with ^{3}H, ^{14}C, and ^{13}C was needed."

Thus, it was an object of Kaspersen et al. to prepare the labeled compounds (see page 1055, item "INTRODUCTION"). In other words, it is thought that the labeled compounds prepared by Kaspersen et al. are to be administered a single time for studies. There is no teaching or suggestion that the labeled compounds are continuously administrated to a patient as a therapeutic substance.

Also, there is clearly no need to use the labeled compounds as pharmaceuticals for humans, and there is no particular advantage disclosed in using the labeled compounds as a therapeutic substance. For example, the compound at page 1058, Fig. 4, which is pointed by the Examiner, is abbreviated as "[$^{13}C_6$]-Org 3770" and denoted as the number of the compound "1c". Also, the compound at page 1067 is abbreviated as "[10-^{14}C]-Org 3770" and denoted as the number of the compound "1d".

Simply put, Kaspersen et al. teach the preparation of these labeled compounds for use in metabolism studies. However, to remove the labels of Kaspersen necessarily renders the compounds *unsuitable for their intended purpose*. As such, there would be no

motivation to modify the labeled compounds of Kaspersen et al. to use them in treatment. Applicants submit that the mere fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness. The prior art must contain a suggestion to make the modification, and there is clearly no suggestion by Kaspersen et al. to make the modifications. The mere fact that a prior art device or process could have been modified, does not make the modification obvious unless the prior art suggested the desirability of the modification. See e.g., In re Gordon, 221 USPQ 1125, 1127 (Fed. Cir. 1984) and Ex parte Tanksley, 37 USPQ2d 1382 (BPAI 1994).

Furthermore, inventive claims 12-15 relate to specific properties of the crystals, for instance, average particle diameter of the crystals or whether or not the crystals are pulverized. Kaspersen contains no disclosure of such limitations. Since the Examiner has made no attempt to specifically address these claims, Applicants respectfully request that the Examiner reconsiders his position regarding these claims. If the Examiner should maintain his position, Applicants respectfully request that the Examiner provides sufficient reasons to conclude that claims 12-15 are *prima facie* obvious.

In addition, the Examiner states at page 3, lines 8-9 of the outstanding Office Action that "[o]ne skilled in the art would not consider the labeled and unlabeled to be in any way significantly different one from the other." Applicants believe that this statement is not supported by any of the art cited by the Examiner, and simply amounts to the Examiner taking "official notice" of a certain fact. Applicants respectfully challenge the above statement, and **request evidence** that the labeled and unlabeled compounds are not in "any way different one from the other," see MPEP 2144.03. Without such evidence, Applicants maintain that there is a significant difference between the labeled and the instant unlabeled compounds.

Lastly, whether or not the crystals of compound 1c are hydrates is for the first time ascertained by examining the physical properties of the crystals of compound 1c.

However, generally, since labeled compounds are not used for therapeutic pharmaceuticals, there is no motivation in Kaspersen et al. to produce and ascertain the physical properties of the labeled compound in order to use unlabeled compounds for therapeutic pharmaceuticals.

Moreover, according to the present invention, an object of the present invention is to provide a compound that is used in

therapeutic pharmaceuticals, in which the labeled compound is not used.

Therefore, it cannot be justified that Kaspersen et al. are applied to the present invention as a cited reference.

Kaspersen et al. do not disclose or suggest hydrates of an unlabeled compound. Moreover, Kaspersen et al. do not disclose or suggest that crystals of compound 1c are hydrates.

Therefore, it is evident that the crystals of an unlabeled compound could not have been expected from Kaspersen et al. by a person skilled in the art.

However, Kaspersen et al. simply disclose the preparation of a labeled compound, and do not disclose or suggest the above facts.

Therefore, it is evident that the present invention cannot be expected from the disclosure of Kaspersen et al.

As specifically explained above, since the present invention could not have been expected from Kaspersen et al. by a person skilled in the art, this rejection should be withdrawn.

Conclusion

In view of the above comments, Applicants respectfully submit that the claims are in condition for allowance. A notice to such a fact is earnestly solicited.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $110.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact **Garth M. Dahlen, Ph.D., Esq.,** (Reg. No. 43,575) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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